ture. Its terms tie in with a series of measures passed by the Legislature and approved by the Governor, all designed to create an orderly unification of the medical and osteopathic professions in the state.

While the unification program has progressed smoothly to date, and while it will remain in effect regardless of the vote on 22, a YES vote on this measure is a must if professional and public confusion are to be eliminated.

This proposition provides that the jurisdiction over those physicians who have now received the M.D. degree and have elected to practice under this discipline shall be transferred to the State Board of Medical Examiners. It further provides that the present Board of Osteopathic Examiners shall have no future right to issue physician-and-surgeon licenses in California by reciprocity or by an initial examination.

The osteopathic board would retain the right to supervise those osteopathic licentiates who have elected to retain the use of the D.O. degree, until such time as the total number of those remaining is decreased to 40. The board would then turn over its final records to the Board of Medical Examiners and go out of business.

This proposition has already been endorsed by both gubernatorial candidates, by both professional associations, by labor and by a large number of civic organizations which have seen the wisdom of maintaining in California only one high standard of medical care. With the endorsements already issued it would appear that there should be no question about getting a YES vote.

On the other hand, there is opposition to this proposal, centering principally in another state where a national organization of osteopaths maintains headquarters. The opposition appears to center its position on the claim of "monopoly." The claim is false; no one is denied access to the kind of medical care he wishes to have and no one is excluded from practice by Proposition 22.

Every physician should know that this ballot proposition is good, is needed for completion of the unification program and is designed to provide the public with whatever is best in medical care. Every physician should work for the passage of this measure and should use his good offices in soliciting votes for it.

Chloramphenicol

SINCE ITS INTRODUCTION in 1948, chloramphenicol has been used clinically with excellent success as a wide-spectrum antibiotic. Annoying side effects such as gastrointestinal intolerance and skin rashes have been virtually absent. However, by 1950 it became evident that it could cause serious and fatal abnormalities in the blood, and the Council on Pharmacy and Chemistry of the American Medical Association in 1954 advised that its use be restricted to the treatment of typhoid fever and other serious infectious diseases caused by chloramphenicol-sensitive microorganisms that are resistant to other antibiotics or to other forms of therapy. Nevertheless, the common use of the drug continued, and fatality sometimes followed. Considering the amount of drug prescribed (net sales in 1959 exceeded $70 million) the incidence of reported aplastic anemia is low.

On the other hand, several recent studies using sensitive hematologic means have indicated that reversible erythroid depression occurs quite frequently in patients receiving chloramphenicol.[2,4] It has been shown that before anemia develops there is a fall in reticulocytes, a rise in serum iron with a decrease in unsaturated iron-binding capacity, a decreased rate of radioiron disappearance from the plasma and a delay in radioiron appearance in new red cells. In the bone marrow, vacuoles appear in the cytoplasm and nuclei of primitive erythroblasts and the number of erythroblasts is decidedly reduced. In one series these changes were found in 16 out of 35 patients whose bone marrow was examined carefully.[4] In each patient blood and marrow reverted to normal after the drug was discontinued. Transient decreases in numbers of white cells and platelets occurred in most of these patients. In another series when chloramphenicol dosage was reduced but not discontinued, serum iron levels returned to normal from previous elevation and bone marrow abnormalities disappeared.[5]

Reversible depression of erythropoiesis following the use of choramphenicol cannot be considered a side reaction; it must be recognized as a pharmacological effect. It is more likely to occur in patients with high levels of chloramphenicol in the blood[1] and in patients with anemia or liver disease. At first it was thought that the nitrobenzene moiety of the chloramphenicol molecule was the cause of the marrow depression. However, when the suspected nitro group was replaced by a methyl sulfone group the incidence of marrow depression actually increased, demonstrating that the nitrobenzene part is not primarily responsible.[3]

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There has been no consistent pattern in the development of severe, irreversible aplastic anemia. Red cells, white cells and megakaryocytes may all be affected. Neither total dosage nor duration of administration nor frequency of therapeutic periods bears a constant relationship to it. Present evidence suggests that factors in the host are important in the development of these changes. Some patients may be unusually sensitive to the pharmacologic effect of the drug, or there may be variations in their nutritional status or differences in absorption, excretion or enzymatic inactivation of the drug. For example, the use of chloramphenicol is particularly hazardous in the newborn: Vasomotor collapse and death may follow use of this antibiotic. In the newborn there is excessive accumulation of chloramphenicol in the blood, since glucuronide conjugation, a normal elimination pathway for this drug, is defective in the immature liver.

It has been suggested that patients who are receiving chloramphenicol should have frequent reticulocyte counts or serum iron determinations to detect evidence of bone marrow depression early. This recommendation is based on the observation that patients in whom reticulocytopenia, a rise in serum iron and changes in bone marrow erythroblasts developed during chloramphenicol therapy, had spontaneous remission of these changes when the drug was discontinued. There is as yet no clear-cut evidence that continued administration of chloramphenicol usually leads to irreversible bone marrow depression, or that early discontinuation is followed invariably by remission. In cases in which chloramphenicol is needed for proper treatment, it actually may be inadvisable to stop giving the drug.

Since the relationship between aplastic anemia and reversible changes in the blood and marrow is as yet unknown and there is no reliable way of predicting the former by examination of the blood, administration of chloramphenicol bears a certain risk. For the time being, it would be advisable to follow the recommendation of the Council on Pharmacy and Chemistry and use the drug only if it is specifically indicated and no other drug can do the job.

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REFERENCES

1. McCurdy, P. R.: Chloramphenicol blood levels and bone marrow toxicity (abstract), Clin. Res., 10:27, 1962.

2. Rubin, D., Weisberger, A. S., Botti, R. E., and Storaasli, J. P.: Changes in iron metabolism in early chloramphenicol toxicity, J. Clin. Invest., 37:1286, 1958.

3. Rubin, D., Weisberger, A. S., and Clark, D. R.: Early detection of drug induced erythropoietic depression, J. Lab. & Clin. Med., 56:453, 1960.

4. Saidi, P., Wallerstein, R. O., and Aggeler, P. M.: Effect of chloramphenicol on erythropoiesis, J. Lab. & Clin. Med., 57:247, 1961.

5. Sampson, W. I., and Wallerstein, R. O., unpublished observations.